SM.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/986,797	11/13/2001	Pascale Briand	03804.0101-02	6235

22852 7590 06/18/2004

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
1300 I STREET, NW
WASHINGTON, DC 20005

EXAMINER	
CHEN, SHIN LIN	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/986,797	BRIAND ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-21 and 23-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-21 and 23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed 4-13-04 has been entered. Claim 22 has been canceled. Claims 14, 19, 23 and 25 have been amended. Claims 14-21 and 23-26 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 14-21 and 23-26 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for expression of beta-galactosidase on the cells of the endothelial layer after anterior chamber injection of the adenovirus, expression of beta-galactosidase on the cells of point of intravitreous injection, and expression of beta-galactosidase on the fibers of the 4 oculomotor muscles after retrobulbar space injection, does not reasonably provide enablement for expressing a gene in at least an eye cell by using a defective recombinant adenovirus expressing a protein or an antisense RNA and expression of said gene via subretinal or intravitreous injection could provide therapeutic effect in vivo for various eye disorders or diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 1-13-04. Applicant's arguments filed 4-13-04 have been fully considered but they are not persuasive.

Applicants argue that the references cited by examiner, concerning the problems and obstacles to achieving efficacious or successful gene therapy, are referring to safety considerations but not enablement requirement. Applicants further cited pages 15-17 of the specification and argue that the specification provides data for successful delivery of a selected gene into cells of the eye with a defective recombinant adenovirus (amendment, p. 6-7). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 1-13-04. The claims encompass administering a defective recombinant adenovirus expressing the gene encoding any protein or antisense RNA to at least an eye cell in vitro or in vivo via subretinal injection and intravitreous injection. The specification discloses expression of beta-galactosidase on the cells of the endothelial layer after anterior chamber injection of the adenovirus, expression of beta-galactosidase on the cells of point of intravitreous injection, and expression of beta-galactosidase on the fibers of the 4 oculomotor muscles after retrobulbar space injection (specification, p. 15-17). It was well known in the art that beta-galactosidase is a marker protein but not a therapeutic protein. The specification fails to provide adequate guidance and evidence for how to use a defective recombinant adenovirus expressing a protein or an antisense RNA to treat an eye disease or disorder, such as ocular disease, via subretinal or intravitreous injection so as to provide therapeutic effect in vivo. The specification also fails to provide adequate guidance and evidence for the correlation between the expressed protein or antisense RNA and a particular eye disease or disorder. The references cited the examiner show that the art of gene therapy in vivo was unpredictable at the time of the invention, many factors influence efficient gene delivery in vivo, and "The Achilles heel of gene therapy is gene delivery, and this is the aspect that we will concentrate on here. Thus, far, the problem has been

an inability to deliver genes efficiently and to obtain sustained expression". Thus, the cited references point out the enablement issues and not just safety issues of gene therapy in vivo.

Applicants cite Bennett reference and argue that subretinal injection of a recombinant replication-deficient adenovirus containing murine cDNA for betaPDE results in delaying photoreceptor cell death by 6 weeks. Applicants further cite posted results in Genvec's website regarding in vivo injection of recombinant replication-defective adenovirus to an eye of a mammal and expression of neurotrophin or PEDF (amendment, p. 7-8). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 1-13-04. The effective filing date of the present invention is 3-3-93 and the publication date of the Bennett reference is June 1996, which is more than 3 years after the effective filing date of the present invention. The published results on the Genvec's website have no publication date. It is unclear when those results were posted on the Genvec's website. Thus, the specification and the state of the art at the time of the invention fail to provide sufficient enabling disclosure to support the claimed invention. Further, as discussed above, the art of gene therapy in vivo was unpredictable at the time of the invention and the claims encompass using defective recombinant adenovirus expressing various protein or antisense RNA to treat various eye diseases or disorders so as to provide therapeutic effect in vivo. Even subretinal injection of a recombinant replication-deficient adenovirus containing murine cDNA for betaPDE can delay photoreceptor cell death in vivo at the time of the invention, gene therapy in vivo using cDNA sequence encoding different protein to treat various eye diseases or disorders has to be considered individually because of the unpredictable nature of gene therapy in vivo. Therefore, the claims remain rejected under 35 U.S.C. 112 first paragraph.

Applicants argue that the specification support successful delivery of a selected gene into cells of the eye with a defective recombinant adenovirus, therefore, it would be successful to delivery antisense RNA (amendment, p. 8-9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 1-13-04 and the reasons set forth above.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.